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Date: July 24, 2002

Page 1 of 4

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| Form PTO-1449 (REV. 07/01) | | U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE | | ATTY. DOCKET NO. SW-046XX | APPLICATION NO. 10 019.816 | | SEP 2 5 2002 |
| INFORMATION DISCLOSURE CITATION (Use several sheets if necessary) | | | | APPLICANT: Michael Valentine Agrez | | | TECH CENTER 1600/2900 |
| | | | | FILING DATE March 27, 2002 | GROUP | | |
| U.S. PATENT DOCUMENTS | | | | | | | |
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| | | | | | | | |
| OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.) | | | | | | | |
| KAC | Agrez, M.V. et al., "Colorectal cancer and the integrin family of cell adhesion receptors: current status and future directions", European Journal of Cancer 30A, 2166-2170 (1994) | | | | | | |
| | Agrez, M.V. et al., "Multiplicity of fibronectin-binding αv integrin receptors in colorectal cancer", Br. J. Cancer 73, 887-892 (1996). | | | | | | |
| | Agrez, M.V., "Cell adhesion molecules and colon cancer", A.N.Z.J. Surgery 66, 789-796 (1996). | | | | | | |
| | Bookstein, R. et al., "p53 gene therapy <i>in vivo</i> for hepatocellular and liver metastatic colorectal cancer", Seminars Oncol. 23, 66-77 (1996). | | | | | | |
| | Boulton, T.G. et al., "ERKs: a family of protein-serine threonine kinases that are activated and tyrosine phosphorylated in response to insulin and NGF", Cell 65, 663-675 (1991). | | | | | | |
| | Cone, R.I. et al., "Effects of beta subunit cytoplasmic domain deletions on the recruitment of the integrin alpha v beta 6 to focal contacts", Cell Adhes. Comm. 2, 101-113 (1994). | | | | | | |
| | Coppolino, M. et al., "Inducible interaction of integrin alpha 2 beta 1 with calreticulin. Dependence of the activation state of the integrin", J. Biol. Chem. 270, 23132-23138 (1995). | | | | | | |
| | Gamble, J.R. et al., "Regulation of <i>in vitro</i> capillary tube formation by anti-integrin antibodies", J. Cell Biol. 121, 931-943 (1993). | | | | | | |
| ✓ | Garrington, T.P. et al., "Organization and regulation of mitogen-activated protein kinase signaling pathways", Curr. Opin. Biol. 11, 211-218 (1999). | | | | | | |

EXAMINER

Form - J. Gamble

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| INFORMATION DISCLOSURE CITATION <i>(Use several sheets if necessary)</i> | | | | APPLICANT: Michael Valentine Agrez | |
| | | | | FILING DATE March 27, 2002 | GROUP |

U.S. PATENT DOCUMENTS

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OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.)

| | |
|------------|---|
| <i>KAL</i> | Giancotti, F.G. et al., "Integrin signalling", Science 285, 1028-1032 (1999). |
| | Gorgziglia and Kapikian, J., Virol. 66, 4407-4412 (1992). |
| | Grammer, T.C. et al., "Evidence for MEK-independent pathways regulating the prolonged activation of the ERK-MAP kinases", Oncogene 14, 1635-1642 (1997). |
| | Guan, J.L. et al., "Regulation of focal adhesion-associated protein tyrosine kinase by both cellular adhesion and oncogenic transformation", Nature 358, 690-692 (1992). |
| | Hannigan, G.E. et al., "Regulation of cell adhesion and anchorage-dependent growth by a new beta 1-integrin-linked protein kinase", Nature 379, 91-96 (1996). |
| | Hemler, M.E., "Integrin associated proteins", Curr. Opin. Biol. 10, 578-585 (1998). |
| | Hergott, G.J. et al., "Inhibition of retinal pigment epithelial cell migration and proliferation with monoclonal antibodies against the beta 1 integrin subunit during wound healing in organ culture", Invest. Ophthalmol. Vis. Sci. 34, 2761-2768 (1993). |
| | Horwitz, A. et al., "Interaction of plasma membrane fibronectin receptor with talin-a transmembrane linkage", Nature 320, 531-533 (1986). |
| | Howe, A. et al., "Integrin signaling and cell growth control", Curr. Opin. Biol. 10, 220-231 (1998). |
| | Knezevic, I. et al., "Direct binding of the platelet integrin alpha lib beta 3 (Gpllla) to talin. Evidence that interaction is mediated through the cytoplasmic domains of both alpha lib and beta 3", J. Biol. Chem. 271, 16416-16421 (1996). |
| ✓ | Kornberg, L. et al., "Cell adhesion or integrin clustering increases phosphorylation of a focal adhesion-associated tyrosine kinase", J. Biol. Chem. 267, 23439-23442 (1992). |

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|----------|------------------------|-----------------|----------------|
| EXAMINER | <i>John J. Camille</i> | DATE CONSIDERED | <i>3/29/05</i> |
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Page 3 of 4

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SW-046XX

APPLICATION

APPLICANT:

Michael Valentine Agtez

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March 27, 2002

U.S. PATENT DOCUMENTS

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FOREIGN PATENT DOCUMENTS

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OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.)

| | |
|----|--|
| KA | Loftus, J.C. et al., "Integrin-mediated cell adhesion: the extracellular face", <i>J. Biol. Chem.</i> 269, 25235-25238 (1994). |
| | Miranti, C.K. et al., "Protein Kinase C regulates integrin-induced activation of the extracellular regulated kinase pathway upstream of Shc", <i>J. Biol. Chem.</i> 274, 10571-10581 (1999). |
| | Oley, C.A. et al., "An interaction between alpha-actinin and the beta 1 integrin subunit in vitro", <i>J. Cell Biol.</i> 111, 721-729 (1990). |
| | Payne, D.M. et al., "Identification of the regulatory phosphorylation sites in pp42 mitogen-activated protein kinase (MAP kinase)", <i>EMBOJ</i> 10, 885-892 (1991). |
| | Pfaff, M. et al., "Integrin beta cytoplasmic domains differentially bind to cytoskeletal proteins", <i>J. Biol. Chem.</i> 273, 6104-6109 (1998). |
| | Reszka, A.A. et al., "Identification of amino acid sequences in the integrin beta 1 cytoplasmic domain implicated in cytoskeletal association", <i>J. Cell Biol.</i> 117, 1321-1330 (1992). |
| | Rojiani, M.V. et al., "In vitro interaction of a polypeptide homologous to human Ro SS-A antigen (calreticulin) with a highly conserved amino acid sequence in the cytoplasmic domain of integrin alpha subunits", <i>Biochemistry</i> 30, 9859-9866 (1991). |
| | Schaller, M.D. et al., "Focal adhesion kinase and paxillin bind to peptides mimicking beta integrin cytoplasmic domains", <i>J. Cell Biol.</i> 130, 1181-1187 (1995). |
| ✓ | Sheppard, D. et al., "Complete amino acid sequence of a novel integrin β subunit ($\beta 6$) identified in epithelial cells using the polymerase chain reaction", <i>J. Biol. Chem.</i> 265, 11502-11507 (1990). |

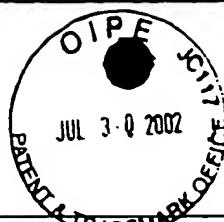
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Karen J. Canella

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Page 4 of 4

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| Form PTO-1449 U.S. DEPARTMENT OF COMMERCE (REV. 07/01) PATENT AND TRADEMARK OFFICE | | | | ATTY. DOCKET NO. SW-046XX | APPLICATION NO. 10-019,816 | | |
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| INFORMATION DISCLOSURE CITATION <i>(Use several sheets if necessary)</i> | | | | APPLICANT: Michael Valentine Agrez | | | |
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OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.)

| | |
|------|---|
| KA C | Varner, J.A. et al., "Integrin alpha 5 beta 3 expression negatively regulates cell growth: reversal by attachment to fibronectin", Mol. Biol. Cell 6, 725-740 (1995). |
| 1 | Wang, A. et al., "Differential regulation of airway epithelial integrins by growth factors", Am. J. Respir. Cell & Mol. Biol. 15, 664-672 (1996). |
| ✓ | Wary, K.K. et al., "The adaptor protein Shc couples a class of integrins to the control of cell cycle progression", Cell 87, 733-743 (1996). |
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| EXAMINER | <i>Norma A. Camila</i> | DATE CONSIDERED | <i>3/29/05</i> |
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Page 1 of 1

| <p>U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE (REV. 08/02)</p> <p>INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)</p> <p><i>O I P E</i> NOV 22 2002 PATENT & TRADEMARK OFFICE U.S. DEPARTMENT OF COMMERCE</p> | | | | ATTY. DOCKET NO. SW-046XX | APPLICATION NO. 10/019.816 | | |
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| | | | | APPLICANT: Michael Valentine Agrez, et al. | | | |
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| U.S. PATENT DOCUMENTS | | | | | | | |
| EXAMINER INITIAL | DOCUMENT NUMBER | PUBLICATION ISSUE DATE | NAME | CLASS | SUBCLASS | FILING DATE | |
| <i>KAC</i> | US 6,007,991 | 12/28/1999 | Sivaraman, et al. | 435 | 6 | <i> </i> | |
| <i>KAC</i> | US 5,593,884 | 1/14/1997 | Karin, et al. | 435 | 252.3 | <i> </i> | |
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| <i>KAC</i> | WO 00/59549 | 10/12/2000 | PCT | | | | |
| <i> </i> | WO 99/09214 | 2/25/1999 | PCT | | | | |
| <i> </i> | WO 91/19008 | 12/12/1991 | PCT | | | | |
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| EXAMINER <i>John A. Canella</i> | | | | DATE CONSIDERED <i>3/29/03</i> | | | |
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Date: July 29, 2002
Page 1 of 1

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| INFORMATION DISCLOSURE CITATION (Use several sheets if necessary) | | O I P E AUG 05 2002 PATENT & TRADEMARK OFFICE | | APPLICANT: Michael Valentine Agrez et al. | | |
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| KAL | WO 92/12236 | 23/7/92 | | | | |
| | | | | | | |
| OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.) | | | | | | |
| KAL | <ul style="list-style-type: none"> Chen et al., "Distinct Structural Requirements for Interaction of the Integrins $\alpha 5\beta 1$, $\alpha v\beta 5$, and $\alpha v\beta 6$ with the Central Cell Binding Domain in Fibronectin", Cell Adhesion and Communication, vol. 4, nos. 4-5, pp. 237-250 (1996). Cone et al., "Effects of β Subunit Cytoplasmic Domain Deletions on the Recruitment of the Integrin $\alpha v\beta 6$ to Focal Contacts", Cell Adhesion and Communication, vol. 2, pp. 101-113 (1994). Coppolino et al., "Bi-directional signal transduction by integrin receptors," The International Journal of Biochemistry & Cell Biology, vol. 32, pp. 171-188 (2000). Dixit et al., "Identification of a Sequence within the Integrin $\beta 6$ Subunit Cytoplasmic Domain That Is Required to Support the Specific Effect of $\alpha v\beta 6$ on Proliferation in Three-Dimensional Culture", J. Biol. Chem., vol. 271, no. 42, pp. 25976-25980 (1996). Gotoh et al., "Cross-Linking of Integrins Induces Tyrosine Phosphorylation of the Proto-Oncogene Product Vav and the Protein Tyrosine Kinase Syk in Human Factor-dependent Myeloid Cells", Cell Growth and Differentiation, vol. 8, pp. 721-729 (1997). Lin et al., "Integrin-mediated Activation of MAP Kinase Is Independent of FAK: Evidence for Dual Integrin Signaling Pathways in Fibroblasts", J. Cell. Biol., vol. 136, no. 6. (1997). Sheppard et al., "Complete Amino Acid Sequence of a Novel Integrin β Subunit (β_n) Identified in Epithelial Cells Using the Polymerase Chain Reaction", J. Biol. Chem., vol. 265, no. 20, pp. 11502-11507 (1990). Yokosaki et al., "Differential Effects of the Integrins $\alpha 9\beta 1$, $\alpha v\beta 5$, and $\alpha v\beta 6$ on Cell Proliferative Responses to Tenascin: Roles of the β Subunit Extracellular and Cytoplasmic Domains," J. Biol. Chem., vol. 271, no. 39, pp. 24144-24150, (1996). | | | | | |
| EXAMINER | Karen D. Canale | | DATE CONSIDERED 3/29/05 | | | |
| *EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | | | | | | |

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PATENT AND TRADEMARK OFFICE Page 1 of 2

| INFORMATION DISCLOSURE CITATION <i>(Use several sheets if necessary)</i> | | | | ATTY. DOCKET NO. | APPLICATION NO. | | |
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| | | | | SW-046XX (now BLAKE-046XX) | 10/019,816 | | |
| | | | | APPLICANT: Michael Valentine Agrez, et al. | | | |
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| FOREIGN PATENT DOCUMENTS | | | | | | | |
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| KH | | ** WO 01/00677 | Publ 1/4/2001 | PCT | | | |
| | | | | | | | |
| OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.) | | | | | | | |
| KH | | Boulton, T.G., et al., "Mitogen-activated protein kinase 1," (EC 2.7.1) (1991) (Swiss Prot Acc No. P27703). | | | | | |
| | | ** Breuss, J.M., et al., "Restricted distribution of integrin β 6 mRNA in primate epithelial tissues," J Histochem Cytochem (1993), 41: 1521-1527. | | | | | |
| | | Carloni, V., et al., "The integrin α 6 β 1, is necessary for the matrix-dependent activation of FAK and MAP Kinase and the migration of human hepatocarcinoma cells," Hepatology 2001, Jul; 34(1): 42-9. (PUBMED ABSTRACT) | | | | | |
| | | ** Eliceira, B.P., et al., "The role of α v integrins during angiogenesis: insights into potential mechanisms of action and clinical development," J Clin Invest (1999), 103(9): 1227-30. | | | | | |
| | | ** Eliceira, B.P., et al., "Integrin α v β 3 requirement for sustained mitogen activated protein kinase activity during angiogenesis," J Cell Biol (1998), 140(5): 1255-63. | | | | | |
| | | ** Friedlander, M., et al., "Definition of two angiogenic pathways by distinct α v integrins," Science (1995), 270(5241): 1500-2. | | | | | |
| | | Gonzales, F.A., " <i>H Sapiens</i> 40kDa protein kinase related to rat ERK2," (1992) (GenPept Acc No. CAA77753). | | | | | |
| | | ** Gupta, K., et al., "VEGF prevents apoptosis of human microvascular endothelial cells via opposing effects on MAPK/ERK and SAPK/JNK signalling," Exp Cell Res (1999), 247(2): 495-504. | | | | | |
| ✓ | | Ishii, T., et al., "Integrin-linked Kinase Controls Neurite Outgrowth in NIE-115 Neuroblastoma Cells," J. Biol. Chem. (2001), 276(46): 42994-43003. | | | | | |
| EXAMINER | <i>Karen A. Gamble</i> | | | DATE CONSIDERED <i>3/28/05</i> | | | |
| *EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | | | | | | | |

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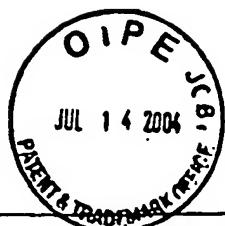


Date: October 23, 2003
Page 2 of 2

| (REV. 05/03) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE CITATION <i>(Use several sheets if necessary)</i> | | | | ATTY. DOCKET NO. | APPLICATION NO. | | |
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| OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.) | | | | | | | |
| KAC | ** Pages, G., et al., "Signaling angiogenesis via p42/p44 MAP kinase cascade," Ann NY Acad Sci (2000), 902: 187-200. | | | | | | |
| | ** Redlitz, A., et al., "Angiostatin diminishes activation of the mitogen-activated protein kinases ERK-1 and ERK-2 in human dermal microvascular endothelial cells." J Vasc Res (1999), 36(1): 28-34. | | | | | | |
| | Sugiura, N., et al., "Mus musculus DNA for ERK2," exon 7 (1997) (GenPept Acc No. BAA22620). | | | | | | |
| | ** Tanaka, K., et al., "Roles of extracellular signal-regulated kinase 1 / 2 and p38 mitogen-activated protein kinase in the signal transduction of basic fibroblast growth factor in endothelial cells during angiogenesis," Jpn J Cancer Res (1999), 90(6): 647-54. | | | | | | |
| ✓ | ** Yu, Y., et al., "MAP kinases, phosphatidylinositol 3-kinase, and p70 S6 kinase mediate the mitogenic response of human endothelial cells to vascular endothelial growth factor," J Cell Physiol (1999), 178(2): 235-46. | | | | | | |
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| EXAMINER | <i>Jamie A. Canale</i> | | | DATE CONSIDERED <i>3/29/05</i> | | | |
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Date: July 12, 2004

Page 1 of 4

| U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE (REV. 05/03) | | | | ATTY. DOCKET NO. | APPLICATION NO. | | |
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| OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.) | | | | | | | |
| KAC | | Agrez, M.V. et al., "The $\alpha\beta\beta$ integrin induces gelatinase B secretion in colon cancer cells," Int. J. Cancer: 81, 90-97 (1999). | | | | | |
| | | Agrez, M., et al., "The $\alpha\beta\beta$ integrin promotes proliferation of colon carcinoma cells through a unique region of the $\beta\beta$ cytoplasmic domain," J. Cell Biol. 127, No. 2, pp 547-556 (October 1994). | | | | | |
| | | Ahmed, N. et al., "Direct integrin $\alpha\beta\beta$ -ERK binding: implications for tumour growth," Oncogene 21, pp 1370-1380 (21 February 2002). | | | | | |
| | | Dedhar, S. et al., "Integrin cytoplasmic interactions and bidirectional transmembrane signalling," Current Opinion in Cell Biology, Current Science, London, vol. 8, no. 5, pp 657-669 (1 October 1996). | | | | | |
| | | Erker, J.C. et al., DATABASE GENBANK 'Online!, "polyprotein GB virus c/Hepatitis C virus," Database accession no. AAC55951 (13 November 1996). | | | | | |
| | | Fodstad, O. et al., "DATABASE GENESEQ 'Online!, "CAPL gene 5' splice site antisense oligonucleotide," Database accession no. AAT33333 (12 November 1996). | | | | | |
| | | Hughes, P.E. et al., "Integrin affinity modulation," Trends in Cell Biology, England, vol. 8, no. 9, pp 359-364 (September 1998). | | | | | |
| | | Kerr, J.S. et al., "Novel small molecule $\alpha\beta$ integrin antagonists: comparative anti-cancer efficacy with known angiogenesis inhibitors," Anticancer Research 19: 959-968 (1999). | | | | | |
| EXAMINER <u>John J. Camella</u> | | | | DATE CONSIDERED <u>3/29/05</u> | | | |
| *EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | | | | | | | |



Date: July 12, 2004

Page 2 of 4

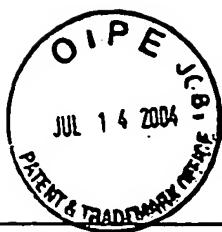
| U.S. DEPARTMENT OF COMMERCE (REV. 05/03) PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE CITATION <i>(Use several sheets if necessary)</i> | | | | ATTY. DOCKET NO. | APPLICATION NO. | |
|--|---|-------------------------|--------------------------------|---|-----------------|-----------------------|
| | | | | BLAKE-046XX | 10/019,816 | |
| | | | | APPLICANT: Michael Valentine Agrez, et al. | | |
| | | | | FILING DATE | TC ART UNIT | |
| | | | | March 27, 2002 | 1651 | |
| U.S. PATENT DOCUMENTS | | | | | | |
| EXAMINER INITIAL | DOCUMENT NUMBER | PUBLICATION/ ISSUE DATE | NAME | CLASS | SUBCLASS | FILING DATE |
| | US | | | | | |
| | US | | | | | |
| FOREIGN PATENT DOCUMENTS | | | | | | |
| | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION YES NO |
| | | | | | | |
| | | | | | | |
| OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.) | | | | | | |
| KAC | Lub, M. et al., "Cytoplasmic tails of β_1 , β_2 , and β_3 integrins differentially regulate LFA-1 function in K562 cells," Molecular Biology of the Cell, vol. 8, no. 4, pp 719-728 (April 1997). | | | | | |
| | Marcantonio, E.E. et al., "Mapping of the functional determinants of the integrin β_1 cytoplasmic domain by site-directed mutagenesis," Cell Regulation, vol. 1, no. 8, pp 597-604 (July 1990). | | | | | |
| | Mastrangelo, A.M. et al., "Amino acid motifs required for isolated β cytoplasmic domains to regulate 'in trans' $\beta 1$ integrin conformation and function in cell attachment," J. Cell Science, vol. 112, no. 2, pp 217-229 (January 1999). | | | | | |
| | Meurers, B.H. et al., DATABASE GENBANK 'Online! "Myosin heavy chain 12 'Homo sapiens!', Database accession no. CAA69036 (8 January 1997). | | | | | |
| | Niu, J. et al., "Integrin expression in colon cancer cells is regulated by the cytoplasmic domain of the $\beta 6$ integrin subunit," Int. J. Cancer, vol. 99, no. 4, pp 529-537 (1 June 2002). | | | | | |
| | Oda, K. et al., DATABASE GENBANK 'Online! "CoxII intron2 ORF 'Marchantia polymorpha!', Database accession no. AAC09431 (2 April 1998). | | | | | |
| | O'Toole, T.E. et al., "Regulation of integrin affinity states through an NPXY motif in the β subunit cytoplasmic domain," J. Biol. Chem. 270, no. 15, pp 8553-8558 (14 April 1995). | | | | | |
| | Pardi, R. et al., "Conserved regions in the cytoplasmic domains of the leukocyte integrin $\alpha_L\beta_2$ are involved in endoplasmic reticulum retention, dimerization, and cytoskeletal association," Journal of Immunology, vol. 155, no. 3, pp 1252-1263 (1 August 1995). | | | | | |
| EXAMINER | <i>John J. Carvalho</i> | | DATE CONSIDERED <i>3/29/05</i> | | | |
| *EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | | | | | | |



Date: July 12, 2004

Page 3 of 4

| DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE <small>(REV. 05/03)</small> | | | | ATTY. DOCKET NO. | APPLICATION NO. | | |
|--|---|-------------------------|---------|--|-----------------|-----------------------|--|
| | | | | BLAKE-046XX | 10/019,816 | | |
| INFORMATION DISCLOSURE CITATION <i>(Use several sheets if necessary)</i> | | | | APPLICANT: Michael Valentine Agrez, et al. | | | |
| | | | | FILING DATE | TC ART UNIT | | |
| | | | | March 27, 2002 | 1651 | | |
| U.S. PATENT DOCUMENTS | | | | | | | |
| EXAMINER INITIAL | DOCUMENT NUMBER | PUBLICATION/ ISSUE DATE | NAME | CLASS | SUBCLASS | FILING DATE | |
| | US | | | | | | |
| | US | | | | | | |
| FOREIGN PATENT DOCUMENTS | | | | | | | |
| | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION YES NO | |
| | | | | | | | |
| | | | | | | | |
| OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.) | | | | | | | |
| KAC | Patil, S. et al, "A double mutation of the NPLY motif in the integrin β_3 cytoplasmic tail abolishes post-ligand binding events of β_3 integrins," Molecular Biol. of the Cell, vol. 7, no. Suppl., p.248A (Annual Mtg. of the 6 th International Congress on Cell Biology and the 36 th American Society for C; San Francisco, California, US, December 7-11, 1996). | | | | | | |
| | Roberts, M.S. et al., "ERK1 associates with α, β_3 integrin and regulates cell spreading on vitronectin," J. Biol. Chem., vol. 278, no. 3, pp 1975-1985 (17 January 2003). | | | | | | |
| | Swanson, R. et al., DATABASE GENBANK 'Online!', "UL97 honolog 'Rhesus cytomegalovirus!', Database accession no. AAC05259 (7 March 1998). | | | | | | |
| | Tada, M. et al., DATABASE GENBANK 'Online!', "homeobox protein BIX3 'Xenopus laevis!', Database accession no AAC61703 (29 September 1998). | | | | | | |
| | Tahiliani, P.D. et al., "The role of conserved amino acid motifs within the integrin β_3 cytoplasmic domain in triggering focal adhesion kinase phosphorylation," J. Biol. Chem., vol. 272, no. 12, pp 7892-7898 (March 21 1997). | | | | | | |
| | Townsend, P.A. et al., " β_1 integrin antisense oligodeoxynucleotides: utility in controlling osteoclast function," Eur. J. Cell Biol., vol. 78, pp 485-496 (July 1999). | | | | | | |
| | Trikha, M. et al., "Role of $\alpha IIb \beta_3$ integrin in prostate cancer metastasis," The Prostate, vol. 35, pp 185-192 (1998). | | | | | | |
| EXAMINER | <i>John J. Tanaka</i> | | | DATE CONSIDERED <i>3/29/05</i> | | | |
| *EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP, 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | | | | | | | |



Date: July 12, 2004
Page 4 of 4

| U.S. DEPARTMENT OF COMMERCE (REV. 05/03) PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE CITATION <i>(Use several sheets if necessary)</i> | | | | ATTY. DOCKET NO. | APPLICATION NO. | |
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| | | | | BLAKE-046XX | 10/019,816 | |
| | | | | APPLICANT: Michael Valentine Agrez, et al. | | |
| | | | | FILING DATE | TC ART UNIT | |
| | | | | March 27, 2002 | 1651 | |
| U.S. PATENT DOCUMENTS | | | | | | |
| EXAMINER INITIAL | DOCUMENT NUMBER | PUBLICATION/ ISSUE DATE | NAME | CLASS | SUBCLASS | FILING DATE |
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| FOREIGN PATENT DOCUMENTS | | | | | | |
| | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION YES NO |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.) | | | | | | |
| KAC | Vignoud, L. et al., "NPXY motifs control the recruitment of the $\alpha 5\beta 1$ integrin in focal adhesions independently of the association of talin with the $\beta 1$ chain," J. Cell Science, vol. 110, pp 1421-1430 (June 1997). | | | | | |
| | Weinacker, A. et al., "Role of the integrin $\alpha_v\beta_6$ in cell attachment to fibronectin, J. Biol. Chem., vol. 269, no. 9, pp 6940-6948 (March 4, 1994). | | | | | |
| | Zage, P.E. et al., "The membrane proximal region of the integrin β cytoplasmic domain can mediate oligomerization," Cell Adhesion and Communication, vol. 5, no. 5, pp 335-347 (1998). | | | | | |
| | Zhang, Z. et al., "Retroviral transfer of antisense integrin $\alpha 6$ or $\alpha 8$ sequences results in laminar redistribution or clonal cell death in developing brain," J. Neuroscience, vol. 18 (17), pp 6928-6938 (September 1, 1998). | | | | | |
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| EXAMINER | <i>Karen G. Camilleri</i> | | DATE CONSIDERED <i>3/29/05</i> | | | |
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